UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

SERIAL NUMBER	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/063,181	05/14/93	PAULSON	

EXAMINER	
J	1413755
ART UNIT	PAPER NUMBER
FONDA,K	8

18M2/0313

KEVIN L. BASTIAN
TOWNSEND AND TOWNSEND KHOURIE AND CREW
STEUART STREET TOWER
ONE MARKET PLAZA, 20TH FLOOR
SAN FRANCISCO, CA 94105

DATE MAILED:
1803

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

03/13/95

☒ This application has been examined ☒ Responsive to communication filed on 8-25-94 4-19-94 ☐ This action is made final.

A shortened statutory period for response to this action is set to expire three month(s), ——— days from the date of this letter.
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. ☒ Notice of References Cited by Examiner, PTO-892.
2. ☒ Notice of Draftsman's Patent Drawing Review, PTO-948.
3. ☒ Notice of Art Cited by Applicant, PTO-1449.
4. ☐ Notice of Informal Patent Application, PTO-152.
5. ☐ Information on How to Effect Drawing Changes, PTO-1474..
6. ☐ _____

Part II SUMMARY OF ACTION

1. ☒ Claims 1-66 and 81-127 are pending in the application.
   Of the above, claims 1-66 and 81-94 are withdrawn from consideration.
2. ☒ Claims 67-80 have been cancelled.
3. ☐ Claims _____ are allowed.
4. ☒ Claims 95-127 are rejected.
5. ☐ Claims _____ are objected to.
6. ☒ Claims 1-66 and 81-127 are subject to restriction or election requirement.
7. ☒ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.
8. ☐ Formal drawings are required in response to this Office action.
9. ☐ The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable; ☐ not acceptable (see explanation or Notice of Draftsman's Patent Drawing Review, PTO-948).
10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____. has (have) been ☐ approved by the examiner; ☐ disapproved by the examiner (see explanation).
11. ☐ The proposed drawing correction, filed _____, has been ☐ approved; ☐ disapproved (see explanation).
12. ☐ Acknowledgement is made of the claim for priority under 35 U.S.C. 119. The certified copy has ☐ been received ☐ not been received ☐ been filed in parent application, serial no. _____ ; filed on _____.
13. ☐ Since this application apppears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.
14. ☐ Other

EXAMINER'S ACTION

PTOL-326 (Rev. 2/93)

SN 08/063181

As Applicant's representative has previously discussed with Examiner Saunders on March 21, 24, and 25, 1994, restriction to one of the following inventions is required under 35 U.S.C. § 121:

I. Claims 1-34, 43-56, 63-66, and 85, drawn to pharmaceutical compositions classified in Class 514, subclass 8+.

II. Claims 35-42, drawn to pharmaceutical compositions containing liposomes, classified in Class 424, subclass 450.

III. Claims 57-62, drawn to pharmaceutical compositions containing immunoglobulins, classified in Class 424, subclass 85.8.

IV. Claims 67-80, drawn to methods for inhibiting selectin-mediated intercellular adhesion, classified in Class 514, subclass 8+.

V. Claims 81-84, drawn to assays for compounds, classified in Class 436, subclass 501, or Class 435, subclass 7.24.

VI. Claims 86-94, drawn to methods for making compounds, classified in Class 530, subclass 345, or Class 536, subclass 124.

The inventions are distinct, each from the other because of the following reasons:

1. Invention I is related to each of Invention II and III as mutually exclusive species in intermediate-final product relationship. Distinctness is proven for claims in this relationship if the intermediate product is useful to make other than the final product (M.P.E.P. § 806.04(b), 3rd paragraph), and the species are patentably distinct (M.P.E.P. § 806.04(h)). In the instant case, the intermediate product is deemed to be useful as a pharmaceutical agent. The inclusion of liposomes or immunoglobulins is not necessary for practice of the invention.
2. Inventions I, II, and III are related to Invention IV as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (M.P.E.P. § 806.05(h)). In the instant case the method may be carried out using non-carbohydrate based selectin-binding compounds.
3. Inventions II and III are distinct from each other because liposomes and immunoglobulins are not related to each other in any particular way. The inventions are

deemed patentably distinct since there is nothing on this record to show them to be obvious variants. Should applicant traverse on the ground that the species are not patentably distinct, Applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the Examiner finds one of the inventions anticipated by the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. § 103 of the other invention.

4. Invention V is distinct from each of the other invention because no compound used in any of the other inventions is required to carry out the claimed assay method.

5. Invention VI is distinct from each of the other inventions because none of the other inventions is directed to the compounds made by Invention VI.

Applicant is further required to elect one of the four species set forth in claim 79, wherein X in claim 78 may be an oligosaccharide, an oligopeptide, a protein, or a lipid.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classifications and/or divergent subject material,

restriction for examination purposes as indicated is proper. Furthermore, searches for the six groups would not be coextensive, and would therefore place an undue burden on the Examiner. A reference for one group could not reasonably be expected also to be a reference for either of the other groups.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 C.F.R. § 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a diligently-filed petition under 37 C.F.R. § 1.48(b) and by the fee required under 37 C.F.R. § 1.17(h).

In response to Examiner Saunders' telephonic restriction requirement, Applicant's representative elected to prosecute Invention IV, claims 67-80, in which X in claim 79 is an oligosaccharide, with traverse. Based on this election, the case was transferred to Examiner Fonda. Applicant's representative has filed a preliminary amendment cancelling elected claims 67-80 and presenting new claims 95-127 in their place. The newly added claims will be examined insofar as they read on oligosaccharide compounds or derivatives thereof which are not oligopeptides, proteins, or lipids. Claims 1-66 and 81-94 are withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b), as being drawn to non-elected inventions.

The drawings are objected to by the Examiner because in Figure 12B, a hydroxyl group appears to be missing from C-2 of the galactose moiety which is bound to neuraminic acid. The drawings are objected to by the Official draftsperson as set forth on enclosed Form 948. Correction is required.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The specification is objected to under 35 U.S.C. § 112, first paragraph, as failing to provide an enabling disclosure.

The specification fails to enable one of ordinary skill in the art at the time of the invention to practice the invention as claimed. It is well known in the biochemical arts in general that ligand/receptor binding is highly specific. In the particular field of selectin-mediated intercellular adhesion, it is known that different selectins have different binding requirements. The Examiner points out that "selectin" is not the name of a specific receptor, but rather is a generic term for a class of receptors having lectin-like domains. The ordinarily skilled worker would have no expectation that a compound which bound one selectin

receptor would be expected also to bind another selectin receptor. Applicant has provided no enabling teaching of the manner in which one would choose which oligosaccharide compound to employ for selective binding of which selectin receptor.

Furthermore, each of claims 95-101, 104, 108, and 120-127 allows for essentially unlimited substitution, especially in terms of the definition of certain variables as "an oligosaccharide". The ordinarily skilled worker would be faced with an undue burden of experimentation in order to determine which particular oligosaccharide derivatives would possess the desired activity, especially in light of the well known highly specific nature of ligand/receptor interactions. Even if a reasonable theoretical prediction of activity could be made based on structural or other considerations, the ordinarily skilled worker is not taught by the specification how to make any conceivable oligosaccharide which might have desirable properties.

Claims 95-127 are rejected under 35 U.S.C. § 112, first paragraph, for the reasons set forth in the objection to the specification.

Claims 109-112 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

In claim 109, the phrase "is an oligosaccharide and" is redundant and should be deleted. Similarly, "is a monosaccharide" should be deleted from claim 110. The phrase "the monosaccharide" in each of claims 111 and 112 should be replaced with --R^3--.

The following is a quotation of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the

time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103.

Claims 95-127 are rejected under 35 U.S.C. § 103 as being unpatentable over LOWE (A).

Applicant claims a method for inhibiting selectin-mediated intercellular adhesion by administration of a carbohydrate compound which selectively binds a selectin receptor.

LOWE teaches (see column 25, line 39, to column 26, line 10) that portions of the Lewis blood group oligosaccharide antigen are known to serve as cell surface receptors, and that such species are "implicated in modulating adhesive events between cells". LOWE suggests the therapeutic use of oligosaccharides as immunomodulators, anti-bacterial agents, and anti-inflammatory agents, by virtue of their ability to block attachment of incompatible blood group antigens, pathogens, or leukocytes to cell surface receptors. LOWE specifically points out inhibition of the interaction between leukocytes and ELAM-1, and its implications for control of the inflammatory response; ELAM-1 is a member of the selectin family of receptors. LOWE does not explicitly recite each of the structures recited in the claims.

It would have been obvious for a person of ordinary skill in the art at the time of the invention, given the teaching of LOWE,

to provide a method for inhibition of selectin-mediated intercellular adhesion which employed oligosaccharide compounds. The Examiner notes that LOWE describes the appropriate oligosaccharides as those based on the "Lewis blood group oligosaccharide antigen", including the fucosyl moiety. LOWE further describes the expected therapeutic benefits to be obtained by administration of such compounds. The oligosaccharide compounds of the claims have the same core structure, including the fucosyl moiety, as the oligosaccharides referred to by LOWE. For these reasons, and also because LOWE had specifically taught that binding to ELAM-1 (a selectin) could be inhibited by such oligosaccharides, the ordinarily skilled worker would have been motivated to prepare oligosaccharides based on the "Lewis blood group oligosaccharide antigen" for the purpose of inhibiting selectin-mediated intercellular adhesion. The Examiner notes that the claims do not require any specific selectin receptor. Selection of appropriate carriers, dosages, and modes of administration would have been well within the level of skill of the worker of ordinary skill in the art at the time of the invention.

Claims 95, 96, 99, 100, 124, and 125 are rejected under 35 U.S.C. § 103 as being unpatentable over LOWE (A) in view of KOSHITOMO, as described in *Chemical Abstracts* (R).

Applicant claims as set forth above, and further that the intercellular adhesion may be associated with an inflammatory condition.

LOWE teaches as set forth above.

KOSHITOMO teaches that oligosaccharide compounds containing the three core monosaccharides recited in instant claim 99 may be used as inflammation inhibitors in general, and as antirheumatics in specific. KOSHITOMO does not state that the mechanism of action of the oligosaccharides is inhibition of selectin-mediated intercellular adhesion.

It would have been obvious for a person of ordinary skill in the art at the time of the invention, to combine the teaching of LOWE with that of KOSHITOMO, and thus provide oligosaccharides having a Gal(1,4)(Fuc(1,3))GlcNAc core for use in a method for inhibition of selectin-mediated intercellular adhesion, which adhesion may be associated with inflammation. The ordinarily skilled worker would have been motivated to employ the compounds of KOSHITOMO in the method taught by LOWE, because LOWE describes the appropriate oligosaccharides as those based on the "Lewis blood group oligosaccharide antigen", including the fucosyl moiety, and KOSHIMOTO's compounds contain such oligosaccharides.

Claims 124 and 125 are rejected under 35 U.S.C. § 103 as being unpatentable over KOSHITOMO, as described in *Chemical Abstracts* (R).

Applicant claims as set forth above.

KOSHITOMO teaches as set forth above.

It would have been obvious for a person of ordinary skill in the art at the time of the invention, given the teaching of KOSHITOMO, to provide oligosaccharides having a Gal(1,4)(Fuc(1,3))GlcNAc core for use in a method for inhibition of selectin-mediated intercellular adhesion associated with inflammation. KOSHITOMO had taught that administration of such compounds was beneficial in the treatment of inflammation. It is not considered relevant that KOSHITOMO may not have recognized the role of selectins in the inflammatory response. The intent of Applicant's claims is clearly a beneficial effect in a patient with regard to inflammation, and KOSHITOMO had taught such an effect. No patentable invention is deemed to reside in discovery of the mechanism by which a result taught in the prior art is achieved.

No claim is allowed.

Papers relating to this application may be submitted to Group 1800 by facsimile transmission. The number of the fax machine located in the Examiner's art unit is (703) 308-4227. The cover

sheet of any document submitted by facsimile transmission should be clearly marked as either an official or an informal communication.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Kathleen Kahler Fonda, at telephone number (703) 308-1620. Examiner Fonda can generally be reached from Monday through Thursday, as well as on alternate Fridays, between 7:30 a.m. and 5:00 p.m. If the Examiner cannot be reached, questions may be addressed to Supervisory Patent Examiner Douglas W. Robinson, at (703) 308-2897. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Kathleen Kahler Fonda, Ph.D.
KKF

DOUGLAS W. ROBINSON
SUPERVISORY PATENT EXAMINER
GROUP 1800